# Secondary interventions following endovascular abdominal aortic aneurysm repair using current endografts. A EUROSTAR report

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***Objective:*** **The purpose of this study was to evaluate the need for secondary interventions after endovascular abdominal aortic aneurysm repair with current stent-grafts.**
***Methods:*** **Studied were data from 2846 patients treated from December 1999 until December 2004. The data were recorded from the EUROSTAR registry. The only patients studied were those with a follow-up of at least 12 months or until they had a secondary intervention within the first 12 months. The cumulative incidences of secondary transabdominal, extra-anatomic, and transfemoral interventions during follow-up (after the first postoperative month) were investigated.**
***Results:*** **A secondary intervention was performed in 247 patients (8.7%) at a mean of 12 months after the initial procedure within a follow-up period of a mean of 23 ± 12 months. Of these, 57 (23%) transabdominal, 43 (16%) involved an extra-anatomic bypass, and 147 (60%) were by transfemoral approach. The cumulative incidence of secondary interventions was 6.0%, 8.7%, 12%, and 14% at 1, 2, 3, and 4 years, respectively. This corresponded with an annual rate of secondary interventions of 4.6%, which was remarkably lower than in a previously published EUROSTAR study of patients treated before 1999. Type I endoleaks (33% of procedures), migration (16%), and rupture (8.8%) were the most frequent reasons for secondary transabdominal interventions. Graft limb thrombosis was the indication for extra-anatomic bypass (60%). Type I endoleak (17%), type II endoleak (23%), device limb stenosis (14%), thrombosis (23%), and device migration (14%) were the most frequent reasons for secondary transfemoral interventions. Operative mortality was higher after secondary transabdominal interventions (12.3%, $P = .007$) compared with transfemoral interventions (2.7%). Overall survival was lower in patients with secondary transabdominal ($P = .016$) and extra-anatomic interventions ($P < .0001$) compared with patients without a secondary intervention.**
***Conclusion:*** **Although the incidence of secondary interventions after endovascular aneurysm repair has substantially decreased in recent years, continuing need for surveillance for device-related complications remains necessary. (J Vasc Surg 2006;43:896-902.)**

Endovascular treatment of abdominal aortic aneurysms (AAA) has been used successfully for more than a decade.[1-3] Recently, two randomized trials demonstrated that aneurysm-related mortality was lower in patients with endovascular repair than in those with open repair of their aneurysm during a follow-up period of 4 years.[2,3] Despite this favorable mid-term outcome, the long-term durability remains a subject of concern, and life-long surveillance to observe satisfactory endograft function is considered essential.[4-8]

Device-related complications such as endoleak and graft migration were frequently observed. These events are associated with an increased risk for aneurysm rupture and therefore need to be identified as early as possible.[9-10] Graft thrombosis may cause also considerable symptoms. These adverse events are repaired by a secondary intervention.[4,11-13]

The incidence of secondary interventions may be considered a surrogate parameter of impending failure of treatment while also representing an important factor to maintain the long-term functionality of the stent-graft repair. Secondary procedures can be categorized according to the invasiveness of the procedure: (1) transabdominal interventions (either with conversion to open repair or with preservation of the endograft), (2) extra-anatomic interventions, and (3) transfemoral interventions.

The need for secondary interventions after endovascular AAA repair had been investigated previously by using the EUROSTAR database.[4] In this previous assessment, however, the study outcome was primarily determined by the early generation stent-grafts. New developments in endograft design most likely will provide better outcome results.[14] In the present EUROSTAR review, the need for secondary interventions according to current treatment was reassessed.

## METHODS

**Design.** The project of European collaborators on stent-graft techniques for AAA repair (EUROSTAR) reg-

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istry was established in February 1996 with the purpose of collating and investigating an extensive multicenter experience on endovascular AAA repair.[15,16] Patients with a nonruptured, asymptomatic infrarenal AAA who underwent elective endovascular repair were prospectively enrolled into the registry after their consent and studied on an intention-to-treat basis. All patients received commercially available CE-approved stent-grafts. The endograft brands that were used in this study included: Zenith (Cook, Bloomington, Ind), Talent (Medtronic/AVE, Santa Rosa, Calif, AneuRx (Medtronic/AVE), Excluder (W. L. Gore and Assoc., Flagstaff, Ariz), Lifepath (Edwards Lifesciences, Irvine, Calif), Fortron (Cordis/Johnson & Johnson, Ft Lauderdale, Fla) Powerlink (Endologix, Irvine, Calif), Ancure (Guidant, Menlo Park, Calif), and Anaconda (Sulzer Vascutech, Inchinnan, United Kingdom).

The EUROSTAR database is maintained on a Web site (www.eurostar-online.org). This site offers data entry facilities to participating physicians (KIKA Medical, Nancy, France), and password-protected access is available for centers and companies to their own data. Alternatively, data submission by fax or mail is available.

The current analysis includes 2846 patients from 131 centers (Appendix, online only). Primary procedures were performed between December 1999 and December 2004. The patients had a minimal follow-up of 12 months unless a secondary intervention occurred before the 12-month visit. These inclusion criteria were similar as in our earlier series. Additional interventions performed at the time of the initial procedure were not counted as secondary procedures. Follow-up visits were scheduled at 1, 3, 6, 12, 18, and 24 months postoperatively and annually thereafter. The aneurysm diameter was determined over the minor axis at the site of the largest cross section. All patients included in the analysis had an aneurysm diameter of ≥40 mm.

The cumulative incidences of secondary interventions were categorized in transabdominal, extra-anatomic, and transfemoral procedures. In patients who underwent multiple procedures, only the most extensive procedure was taken into account, and if two interventions of equal extent were performed, the first one was considered the index intervention.

Secondary interventions were correlated with findings at computed tomography examination and clinical assessment during follow-up to assess for reintervention. Indications included device migration, different types of endoleak, thrombosis, stenosis, kinking of endograft limbs, and rupture of the aneurysm. In addition, procedure-related mortality (defined as death ≤30 days of the secondary intervention) and the all-cause mortality during follow-up were compared among the three types of reinterventions. Reporting was in accordance with the guidelines of the ad hoc Committee for Standardized Reporting Practices in Vascular Surgery of The Society for Vascular Surgery/American Association for Vascular Surgery.[17]

**Statistical analysis.** Kaplan-Meier life tables were used to draw cumulative incidence and survival curves for all types of secondary interventions. Values were represented as means ± standard deviation and ranges. Relative risk ratios (RR) were calculated to correlate secondary interventions with their indications in the follow-up visit preceding reintervention. Multivariate logistic regression was performed for independent comparisons of operative 30-day mortality. The multivariate Cox proportional hazards model was used to calculate independent associations with survival during the postoperative and entire follow-up period. $P < .05$ was considered statistically significant. Analysis was performed by using SAS (version 8.0) statistical software (SAS Institute Inc, Cary, NC).

**Table I.** Endograft devices

| | *Patients with secondary procedure (%)** |
|---|---|
| Zenith[†] | 91/1147 (7.9) |
| Talent[‡] | 77/791 (9.7) |
| Excluder[§] | 25/421 (5.9) |
| AneuRx[‡] | 29/264 (11.0) |
| Lifepath[‖] | 12/67 (17.9) |
| Fortron[¶] | 2/52 (3.8) |
| Powerlink[#] | 6/51 (11.8) |
| EVT[**] | 1/36 (2.8) |
| Anaconda[††] | 4/17 (23.5) |

*Percentage of endoprotheses of each device brand with secondary intervention
†Cook Inc, Bloomington, Ind.
‡Medtronic Corp, Santa Rosa, Calif.
§W. L. Gore and Associates, Inc., Flagstaff, Ariz.
‖Edwards Lifesciences, Irvine, Calif.
¶Cordis/Johnson & Johnson, Fort Lauderdale, Fla.
#Endologix, Irvine, Calif.
**Guidant Inc, Menlo Park, Calif.
††Sulzer Vascutek Ltd., Inchinnan, United Kingdom.

## RESULTS

The 2846 patients who constituted the study group had a mean age of 72.0 ± 7.5 years (range, 43 to 100 years) at the time of the primary procedure. The Zenith endograft was the most frequently used device (40%), followed by Talent (28%) and Excluder (15%) (Table I). The mean length of follow-up was 23 ± 12 months (range, 1 to 60 months). During the follow-up period, the mean AAA diameter shrunk from 58 to 51 mm. Most of the patients were classified as American Society of Anesthesiologists (ASA) grade II or III (Table II). In 1755 patients (62%), the maximum transverse diameter of the aneurysm was ≥5.5 cm, and 1091 patients (38%) had an aneurysm between 4 and 5.5 cm.

Secondary interventions were performed in 247 patients (8.7%) at a mean time of 12 ± 13 months (range, 1 to 48 months) after the initial procedure. There was no significant difference in the rates of reintervention between the different stent-graft labels or bifurcated or aortouniiliac endograft configuration. In large aneurysms (≥5.5 cm), the incidence of secondary interventions after 2 years (9.9%) was higher than in small aneurysms (9.9% compared with 7.1%, Kaplan-Meier analysis $P = .0348$). No other morphologic parameters were found to correlate with the

**Table II.** Baseline characteristics

| *Characteristic* | *All patients** | *Patients with secondary procedure** |
|---|---|---|
| Age at initial procedure (yrs) | 72.0 (43-100) | 71.8 (48-89) |
| Gender | | |
| Males | 2688 (94) | 233 (94) |
| Females | 158 (5.6) | 14 (5.7) |
| Maximum AAA diameter (mm) | 58.3 (40-110) | 60.0 (40-102) |
| ASA Physical status | | |
| I | 249 (8.8) | 21 (8.5) |
| II | 1299 (46) | 112 (45) |
| III | 1127 (40) | 101 (41) |
| IV | 152 (5.4) | 13 (5.3) |

*AAA,* Abdominal aortic aneurysm; *ASA,* American Society of Anesthesiologists.
*Values are represented as mean and range or as number and percentage.

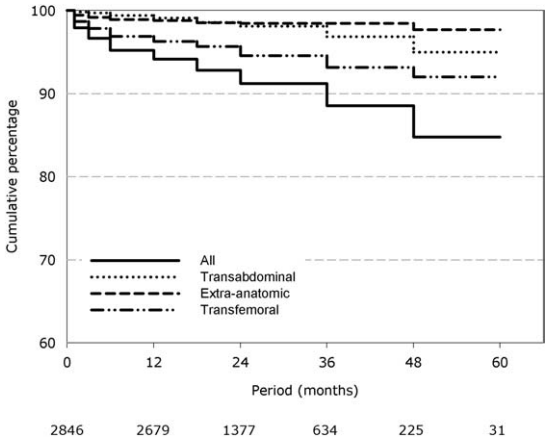


**Fig 1.** Freedom from secondary interventions.

incidence of secondary interventions. In aneurysms without endoleaks (completely excluded), the incidence of secondary intervention after 2 years was lower than in patients with endoleaks at the completion angiogram (8.2% compared with 12.0%, $P = .0133$). Follow-up continued for a mean of 11 ± 12 months (range, 0 to 47 months) after the secondary intervention.

A transabdominal approach was used for 57 of the interventions (23%), 43 procedures (16%) involved extra-anatomic exposure, and 147 interventions (60%) were transfemoral procedures. The cumulative incidence of all secondary interventions in the entire patient cohort was 6.0%, 8.7%, 12%, and 14% at 1, 2, 3, and 4 years respectively (Fig 1). This corresponded with an annual rate of 4.6%.

**Transabdominal secondary interventions.** Conversion to open AAA repair constituted 40 of the 57 secondary transabdominal interventions. In 17, the endograft was preserved, which involved a banding procedure for endoleak, iliofemoral bypass, or laparoscopic clipping. The cumulative incidence of secondary transabdominal interventions was 0.9%, 1.9%, 3.2%, and 5.0% at 1, 2, 3, and 4 years, respectively.

The indications for conversion to open surgical repair were rupture of the aneurysm in 5 (RR, 34.1), device migration in 8 (RR, 24.2), type I endoleak in 10 (RR, 20.1), aneurysmal growth in 14 (RR, 14.6), and endograft infection in 3 (RR, 71.2) (Table III). Eight patients had more than one indication, and no indication was given in five patients. The indications for secondary transabdominal interventions with preservation of endograft function were type I endoleak in five patients (RR, 28.3), thrombosis in two (RR, 43.1), and aneurysmal growth in five (RR, 12.4). Three patients had more than one indication, and no indication was given in one patient.

**Extra-anatomic secondary interventions.** Most of the extra-anatomic procedures (28 of 43) consisted of femorofemoral crossover bypasses. In a few patients, axillofemoral bypasses were used. The cumulative incidence of secondary extra-anatomic interventions was 1.2%, 1.6%, and 2.3% at 1, 2, and 4 years, respectively. The most frequent indication for a secondary extra-anatomic bypass graft was graft thrombosis in 24 cases (RR, 78.5) (Table III). Further indications were type I endoleak in five (RR, 9.0) and stenosis in six patients (RR, 53.4). Two patients had more than one indication, and no indication was given in three patients.

**Transfemoral secondary interventions.** Secondary transfemoral interventions consisted of 76 additional stent-graft or stent placements, including endograft limb extensions, stenting using bare stent or endovascular conversion to an aortouniiliac endograft, 30 coil embolizations of endoleak, 10 thrombectomies, and 13 angioplasty procedures. In 18 patients, the type of secondary transfemoral intervention was not specified. The cumulative incidence of secondary transfemoral interventions was 3.7%, 5.4%, 6.8%, and 8.0% at 1, 2, 3, and 4 years, respectively. All device-related complications that were assessed during follow-up correlated significantly with the use of secondary transfemoral interventions. Type I endoleak was present in 25 patients (RR, 9.5), type II endoleak in 34 (RR, 3.9), type III endoleak in 12 (RR, 6.9), kinking in 9 (RR, 11.1), stenosis in 20 (RR, 19.5), thrombosis in 23 (RR, 17.4), device migration in 20 (RR, 10.9), aneurysmal growth in 15 (RR, 3.2), and rupture in 2 (RR, 4.7). More than one indication was present in 22 patients. The indication for the secondary intervention was unknown in 15 patients.

**Risk factors for secondary intervention.** Independent baseline risk factors for secondary interventions were a required adjuvant procedure ($P = .0001$), proximal endoleak ($P = .0040$), and midgraft endoleak ($P = .0170$) evident at the primary procedure. Patient age, gender, ASA risk classification, systemic comorbidities, type of device, and preoperative aneurysm diameter with thresholds at 5.5, 6.0, and 6.5 cm were not independent risk factors for a secondary intervention.

**Secondary interventions and associated mortality.** The operative mortality rate after transabdominal reintervention was 12.3%. This was significantly higher than the

**Table III.** Indications for secondary interventions.

| *Indication* | *Total** | *Conversion* | *Other transabdominal* | *Extra-anatomic* | *Transfemoral* | *No intervention* |
|---|---|---|---|---|---|---|
| Type I endoleak | 144 | 14 | 5 | 5 | 25 | 95 |
| Type II endoleak | 370 | 7 | 6 | 4 | 34 | 319 |
| Type III endoleak | 101 | 4 | 2 | 2 | 12 | 81 |
| Thrombosis | 68 | 2 | 2 | 24 | 23 | 17 |
| Stenosis | 32 | — | 0 | 6 | 20 | 6 |
| Migration | 73 | 8 | 1 | — | 20 | 44 |
| Kinking | 40 | 1 | — | 5 | 9 | 25 |
| AAA growth | 43 | 14 | 5 | 3 | 20 | 1 |
| AAA rupture | 13 | 5 | — | — | 2 | 6 |
| Bleeding/hematoma | 8 | 2 | 1 | — | 2 | 3 |
| Graft infection | 3 | 3 | — | — | — | — |
| Unknown | — | 5 | 1 | 3 | 15 | — |

*AAA,* Abdominal aortic aneurysm.
*Patients may have more than one indication.

operative mortality rate of 2.3% for patients with extra-anatomic and 2.7% for transfemoral secondary interventions ($P = .0069$). Six patients died after conversion to open repair (15.0%), and one patient died after an endograft-saving transabdominal intervention (5.9%). The difference between these two was not significant ($P = .34$). Considering only conversions to open repair, operative mortality was significantly higher than for less invasive reinterventions, such as extra-anatomic and transfemoral procedures combined ($P = .0009$). The difference between endograft-saving transabdominal intervention and the combined group with extra-anatomic and transfemoral interventions was not significant.

The all-cause mortality rate was higher for both secondary transabdominal interventions ($P = .0157$, hazard ratio, 2.6; 95% confidence interval, 1.2 to 5.5) and extra-anatomic interventions ($P = .0001$, hazard ratio, 2.0; 95% confidence interval, 1.4 to 2.9) compared with patients without a secondary intervention, independent of patient age, fitness, endoleaks, and all graft-related complications, as assessed by multivariate Cox regression. The 3-year survival rates were 80.5%, 62.5%, and 86.2% for patients with transabdominal, extra-anatomic, and transfemoral reinterventions, respectively (Fig 2). All deaths after transabdominal reinterventions were operative death ≤30 days of the secondary procedure; no further deaths occurred. Seven patients who underwent extra-anatomic reinterventions died of unrelated causes, and one died perioperatively. The mortality rate for patients who underwent secondary transfemoral interventions was not higher than for patients without reinterventions. Ten patients who underwent transfemoral reintervention died of unrelated causes, one died of aneurysmal rupture, and three died of procedure-related causes. The difference in mortality rate between transabdominal and extra-anatomic reinterventions was not significant ($P = .33$).

## DISCUSSION

The main finding of the current study was a markedly reduced annual rate of secondary interventions compared with the earlier EUROSTAR experience reported on the patient series who had operations before December 1999 (4.6% vs 9.1%).[4] In 8.7% of patients, a secondary procedure was performed at some time during follow-up in contrast to 18% of patients in the early experience. A survey of 15 studies demonstrated secondary interventions in 17% of patients (683/3905) with endovascular aneurysm repair, ranging from 10% to 34%, which was higher than in the current study.[6,7,11-13,18-27] This is in agreement with our present results and suggests that the need for secondary interventions has tended to decline in recent years.

The lower rate of secondary interventions compared with earlier implanted stent-grafts may be explained by improved stent-graft design[14] and by increased experience of the physicians.[28] In grafts of early design, a considerably higher secondary intervention rate of 48% to 54% was reported.[13,29] The main differences in baseline variables between the two study periods included use of current devices in 100% compared with 26% and a median patient age of 72 vs 69 years in the present and previous overview, respectively. Other variables, including the median aneurysm diameter, were similar in both studies.

There was a trend towards a higher relative proportion of transabdominal and extra-anatomic reinterventions compared with our earlier series (23% and 17% of the total number of secondary procedures vs 12% and 11%, respectively). This trend was largely due to a significant decline in the need for secondary transfemoral interventions compared with the earlier experience, whereas the need for surgical procedures had not significantly decreased. However, the most frequently performed reinterventions still consisted of transfemoral procedures. In contrast with our findings, Flora et al[13] reported a shift from open to endovascular secondary interventions. In their experience, more complications were managed by endovascular techniques over time when they compared the outcome in two study periods. In addition, a decreased incidence of device-related complications was observed in the more recent period, suggest-

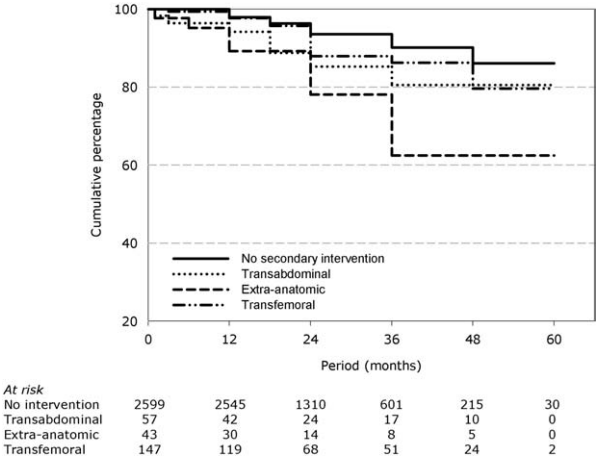


**Fig 2.** Survival.

ing that this type of complication was increasingly dealt with by endovascular technique.

Similar to Sampram et al,[12] proximal type I endoleak evident on the completion angiogram was predictive of later secondary interventions. They found that the incidence of secondary interventions correlated with the aneurysms with the largest diameter and whether the patient was treated later in the study period. The given explanation was that reinterventions were performed more aggressively in large aneurysms and increased over time with more anatomically challenging cases. We could not confirm the aneurysm size, and we found an opposite association for the frequency of reinterventions over time. This was in agreement with their expectation that newer devices might diminish the rate of secondary procedures.

Transabdominal and extra-anatomic procedures were more risky for the patient, as these procedures generally were associated with a higher mortality rate. Extra-anatomic procedures had an increased risk of late death independent of patient fitness and prothrombotic state, and transabdominal procedures were associated with increased operative mortality. The mortality rate of 15% after secondary conversion to open repair was high and exceeded the perioperative mortality rate after elective open repair.[30,31] This observation was in agreement with the findings in other studies ranging from 0% to 40%[11,12,18,21,22,26,32-34] but is lower than the reported 24.4% mortality after secondary conversion in the earlier EUROSTAR experience.[9] When a transabdominal reintervention was survived for the first month, no further deaths during continued follow-up were recorded in the present study cohort. This suggests that patients who were medically fit were selected for an open secondary intervention.

From the previous EUROSTAR and other studies, a considerable amount of device-related complications are known to occur for which no reinterventions are performed.[16,19] Some of these will be managed conservatively, and there is a consensus that type II endoleaks without aneurysm growth should be treated expectatively.[35] Other endoleaks and graft complications may intentionally be left untreated because the patient is unfit. Most physicians will agree, however, that a secondary intervention is definitely indicated in case of aneurysm growth, whereas the complication may only be observed in shrinking aneurysms.

Some patients in the EUROSTAR cohort were awaiting intervention that had been planned, but was not yet performed, and some reinterventions may have yet to be reported because of delay in follow-up data entry. This may underestimate the incidence of secondary interventions. On the other hand, some secondary interventions were performed without a recorded indication (ie, missing information). This under-reporting of indications is a weakness of a voluntary registry such as EUROSTAR. Elaborate case record forms may cause poor compliance of participants, and the follow-up form that was used represented an unavoidable compromise.

Further limitations included possibly a lack of consecutive patient entry. Because patient enrolment was voluntary, it was not known how many centers did not enroll all of their patients but only selected cases. From personal communication with participating centers, we suppose that most did enroll consecutive cases, at least for the period of participation in the registry. An additional aspect that may have influenced the observed rate of secondary interventions was the exclusion from our analysis of patients that had an uneventful follow-up period of <1 year. The reasons for this were:

1. The requirement of a secondary intervention is a function of follow-up time. Including many patients with short follow-up would have resulted in a relative lower rate, whereas we wanted to avoid a picture that was too positive regarding the need of secondary interventions.
2. A comparison of the rates of performed reinterventions with the outcomes in our previous publication[4] was considered most important. That substantially lower secondary intervention rates were found indicates the positive effect of the use of current generation stent grafts.

Accurate parameters that define the need for secondary interventions to treat endoleaks have not yet been fully established.[13] Expansion of the aneurysm sac is, however, an accepted indication for reintervention.[36] In the present study, aneurysm expansion was observed in 17% of patients with secondary interventions, and it was the only reason in 10%.

## CONCLUSION

The incidence of secondary interventions after endovascular aneurysm repair had decreased significantly in recent years. This decrease was mostly due to a lower incidence of transfemoral secondary procedures. Transabdominal and extra-anatomic reinterventions had relatively decreased less and were associated with an

increased mortality risk. Continuing need for surveillance with regard to device-related complications remains necessary.

## AUTHOR CONTRIBUTIONS

Conception and design: RH, JB
Analysis and interpretation: RH
Data collection: RH
Writing the article: RH
Critical revision of the article: JB
Final approval of the article: RH, JB
Statistical analysis: RH
Obtained funding: JB
Overall responsibility: JB

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*Additional material for this article may be found online at www.jvascsurg.org.*

**Appendix (online only)**

The EUROSTAR Collaborative Centers are:

***Belgium:*** Aalst, ASZ and OLV Hospital; Antwerpen, AZ Middelheim, St Vincentius Hospital, UIA, Monica Hospital/OLV/Eeuwfeestkliniek, and St Augustinus Hospital; Assebroek, AZ St Lucas/St Jozef; Baudour, Reseau Hospital de Medecine Sociale; Bonheiden, Imelda Hospital; Brasschaat, AZ Klina; Brugge, AZ St Jan AV; Brussels, Hospital Erasme, Academic Hospital VUB, Clinique de l'Europe St Michel, CHU Brugmann, and Hospital d'Iris Sud; Charleroi, CHU; Dendermonde, AZ St Blasius; Duffel, AZ St Maarten; Geel, AZ St Dimpna; Genk, St Jan Hospital; Gent, Volkskliniek, AZ St Lucas, St Jan Palfijn, University Hospital, and AZ ia Middelares/St Jozef; Gilly, St Joseph Hospital; Haint Saint Paul, Hospital de Jolimont; Halle, Regional Hospital St Maria; Hasselt, Virga Jesse Hospital; Herenthals, St Elisabeth; Ieper, Regional Hospital Yperman; Knokke, VZW Gezondheidszorg Oostkust; Kortrijk, AZ Groenige; Leuven, University Hospital and Heilig Hart; Liège, University Hospital and Clinique Saint-Joseph; Liège-Chenee, Notre-Dame des Bruyeres; Lommel, Maria Hospital; Mechelen, OLV Hospital; Menen, Heilig Hart; Merksem, Jan Palfijn; Mons, St Joseph Warquignies; Mont Godinne, De Mont Godinne; Mouscron, CHM CNDT; Namur, Clinique St Elisabeth; Ottignies, Clinique Saint-Pierre; Reet, AZ Heilige Familie; Roeselare, Stedelijk Hospital and HHR Hart Hospital; Sambreville, CHR Val de Sambre; St Truiden, St Trudo Hospital; Tielt, St Andries Hospital; Tournai, Clinique Notre Dame et St Georges; Turnhout, St Josef Hospital and St Elisabeth; Veurne, St Augustinus Hospital; and Vilvoorde, St Josef Hospital.

***Denk:*** Odense, University Hospital.

***France:*** Paris, Hospital Henri Mondor.

***Germany:*** Frankfurt, Städtischen Kliniken and Cardioangiologisches Centre Bethanien; Hamburg, Altona General Hospital; Kempten, Klinikum Kempten; Koblenz, Bundeswehrzentral; Leipzig, Park-Krankenhaus; Marburg, Philipps-University; München, Kliniken Rechts der Isar; and Oldenburg, Pius Hospital.

***Ireland:*** Dublin, St James Hospital.

***Israel:*** Tel Aviv, Sheba Medical Centre.

***Italy:*** Perugia, Policlinico Monteluce; Roma, Ospedale S Giovanni; and Varese, Ospedale di Circolo Varese.

***Luxembourg:*** Luxembourg, Centre Hospitalier.

***Monaco:*** Monaco, Centre Cardio-Thoracique.

***The Netherlands:*** Alkmaar, Medical Centre; Amsterdam, Academic Medical Centre and OLV, Gasthuis; Arnhem, Rijnstate; Dordrecht, Albert Schweitzer Hospital; Eindhoven, Catharina Hospital; Enschede, Medisch Spectrum Twente; Geldrop, St Anna Hospital Groningen; Academic Hospital and Martini Hospital; Maastricht, Academic Hospital; Nieuwegein, St Antonius Hospital; Nijmegen, CWZ Hospital and Academic Hospital St Radboud; Rotterdam, St Clara Hospital, Dijkzicht Hospital, and Franciscus Gasthuis; The Hague, Leijenburg Hospital; Tilburg, Elisabeth Hospital and Tweesteden Hospital; Utrecht, University Medical Centre; Veldhoven, St Josef Hospital; and Zwolle, Isala Clinics Sophia.

***Norway:*** Oslo, Aker University Hospital and Ulleval Hospital; and Trondheim, University Hospital.

***Poland:*** Lublin, L'Academie de medicine; and Warsaw, Medical University.

***Spain:*** Barcelona, University Hospital, Ciutat Sanitaria I Universitaria de Bellvitge, and Hospital Santa Creu I S Pau; Donostia San Sebastian, Hospital de Gipuzkoa; La Coruña, Hospital Juan Canalejo; Leon, Hospital de Leon; Lugo, Hospital Xeral Lugo; Madrid, University Hospital de la Princesa, Virgen de la Salud, Hospital Ramon y Cajal, Fundacion Jimenez Diaz;, and University Hospital of Getafe; Malaga, HR Carlos Haya; Pamplona, University Hospital of Navarra; and Valladolid, Hospital Clinico Valladolid.

***Sweden:*** Örebro, Medical Centre.

***Switzerland:*** Bern, Clinic for Cardiovascular Surgery.

***United Kingdom:*** Bournemouth, Royal Hospital; Glasgow, Gartnavel Hospital; Liverpool, Royal University Hospital; Manchester, Withington Hospital; and New Castle-Upon-Tyne, Freeman Hospital.